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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,701	02/25/2000	JOHN P. LEONARD	GI5229FWC-DIV1	7087

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EXAMINER

MINNIFIELD, NITA M

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 07/15/2003

25

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/512,701	LEONARD ET AL.
	Examiner	Art Unit
	N. M. Minnifield	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) Responsive to communication(s) filed on 23 April 2003.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 16 and 18-43 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 16 and 18-43 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)  The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 21, 23.

4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

1. Applicants' amendment filed April 23, 2003 is acknowledged and has been entered. Claim 17 has been canceled. Claims 23 and 24 have been amended. New claims 32-43 have been added. Claims 16 and 18-43 are now pending in the present application. All rejections have been withdrawn in view of Applicants' Response with the exception of those discussed below.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Claims 23, 24, 33-37 and 39-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 23 recites, "antibody that binds to IL-12 binds to an epitope on a 40 kD subunit of IL-12" and claim 24 recites, "antibody that binds to IL-12 binds to an epitope on a 35 kD subunit of IL-12". Claims 33-37 recite the limitation of "(a) blocks the formation of a heterodimer containing the 40 kD subunit; or (b) allows the formation of a heterodimer containing the 40 kD subunit, but blocks the activity of said heterodimer". Claims 39-43 recite the limitation of "(a) blocks the formation of a heterodimer containing the 35 kD subunit; or (b) allows the formation of a heterodimer containing the 35 kD subunit, but blocks the activity of said heterodimer". The specification does not set forth enablement for any of

these now claimed limitations. A review of page 8, line 5 through page 9, line 22 of the specification (as indicated by Applicants to show support for the claim amendments and new claims) does not set forth support for the claim limitations. The specification, at pages 8-9, does not set forth the epitope on the 40 kD or 35 kD subunit of the IL-12, nor does it set forth a description or enablement for blocking the formation of the heterodimer or forming the heterodimer.

4. Claims 23, 24 and new claims 32-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using an IL-12 antibody, does not reasonably provide enablement for use of an antibody binds to a 40 kD or 35 kD subunit of IL-12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification has not taught such an antibody that only binds to the 40 kD or 35 kD subunit of the IL-12 or binds to an epitope on a 40 kD or 35 kD subunit of IL-12 and will still be able to treat rheumatoid arthritis or any autoimmune condition (for disease condition see claims 34-36 and 40-42) in a human.

The rejection is maintained for the reasons of record. Applicant's arguments filed October 16, 2002 have been fully considered but they are not persuasive. Applicants have asserted that the specification provides an example of how IL-12 antibody can be used to treat an animal model of MS showing that it does, in fact, decrease levels of IFN- production, and that one of skill in the art would be able to use this invention as disclosed and optimize it with undue experimentation, to treat RA, another condition that benefits in the reduction of IFN- levels. Although the specification does not specifically set forth IL-12

antibodies administered to a animal or human to treat RA, it would be reasonable to one skilled in the art that IL-12 antibody could be used to treat RA in a similar manner as IL-12 antibody is used to treat MS, for the reasons given by Applicants. It would appear that the anti-IL-12 antibodies would decrease the IFN- production and thus be able to treat RA, since Applicants and the prior art suggest that IFN- production promotes several autoimmune conditions including MS and RA. The prior art suggests that IL-12 expression is required for disease progression (CIA, collagen-induced arthritis, an animal model of RA) and inhibition of IL-12 with mAb prevents disease progression (Peeva et al, 2000).

However, the specification does not enable the claims set forth in this rejection. Claims 23 and 24 are directed to treatment of RA by administering an antibody that binds to a 40 kD or 35 kD subunit of IL-12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification has not taught such an antibody that only binds to the 40 kD or 35 kD subunit of the IL-12 and will still be able to treat rheumatoid arthritis in a human or animal. Applicants have pointed to portions of the specification for support that appear to be a mere paper protocol for a method of treating RA that administers an antibody that binds to a 40 kD or 35 kD subunit of IL-12 (IL-12 subunit “may be used”; pp. 6-8). Kim et al (2000) teaches that IL-12 levels reflect RA disease activity and that IL-12 is involved in the production of proinflammatory cytokines. An IL-12 blockade (i.e. anti-IL-12 antibodies) could be useful for the treatment of RA. Kim et al also teaches that the IL-12 is composed of the p35 and p40 subunits, but that neither of these (p35 or p40)

subunits has been found to display any significant biological function alone (p. 175).

Applicant's arguments filed April 23, 2003 have been fully considered but they are not persuasive. Applicants have asserted that none of claims 23 or 24 require that the antibody bind only the 40 kD or the 35 kD subunit of the IL-12 heterodimer. However, the claims are directed to the antibody to IL-12 binding specifically to an epitope on a 40 kD subunit or 35 kD subunit of IL-12. The specification does not enable such; the specification does not define the epitope of the 40 or 35 kD subunit of the IL-12. Further, Benson et al, 2002 appears to indicate that IL-12 may not have a dominant role in chronic autoimmune diseases but rather IL-23. The IL-12p40 is shared by IL-23, a heterodimeric cytokine. Benson et al found that IL-12 specific neutralization had no beneficial effect on progression of experimental autoimmune encephalomyelitis (EAE), but that neutralization of both IL-12 and IL-23 effectively ameliorated EAE clinical signs. Therefore it is difficult to predict which antibody to the subunits of these cytokines (IL-12 or IL-23) or epitopes of the subunits of these cytokines binding to IL-12 are effective in a method of treating autoimmune diseases, without experimental evidence.

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214

USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16 and 18-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-20 of co-pending Application No. 09/512930. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications claim methods of administering to a subject a therapeutically effective amount of an IL-12 antagonist (i.e. antibody immunoreactive with IL-12 or antibody fragment immunoreactive with IL-12); the antagonist is being administered for the purpose of treating conditions promoted by an increase in levels of interferon-gamma, which encompasses autoimmune diseases such as rheumatoid arthritis or multiple sclerosis.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

*The terminal disclaimer filed on April 23, 2003 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the*

*expiration date of US Application 09/512930 has been reviewed and is NOT accepted. M. Andrea Ryan is not authorized to act on behalf of assignee.*

6. No claims are allowed.

7. The information disclosure statement filed April 23, 2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

The Examiner will consider references that have not been initialed if a copy of the references is provided along with the response to this Office Action.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 703-305-3394. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



N. M. Minnifield

Primary Examiner

Art Unit 1645

NMM

July 7, 2003